UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,303	07/26/2006	Chi Vu	A1 38 US 002	6386

7590 12/01/2006

Biogen Idec Inc
Patent and Trademark Coordinator
14 Cambridge Center
Cambridge, MA 02142

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/552,303	VU ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,25-32,36 and 40-51* is/are rejected.

7)☒ Claim(s) *2-24, 33-35 and 37-39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-51 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Parkinson's disease does not reasonably provide enablement for treatment all or any disease central nervous system diseases, as embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims 40-43 are drawn to a method of modulating and inhibiting adenosine-A_{2a} receptors while claims 44-51 are drawn to a method of treating or preventing a disorder or disease in which adenosine-A_{2a} receptors are associated with.

Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition or modulation of adenosine-A_{2a} receptors by the instant compounds, instant claims reaches through inhibiting and

treating any or all diseases and disorders in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor or modulator of adenosine-A_{2a} receptors, based on limited assay, it is claimed that treating or preventing any or all diseases or disorders in general, which there is no enabling disclosure. The scope of the claims include both treating and preventing any or all diseases/disorders due said mode of action for which there is no enabling disclosure.

Reading from specification these include neurodegenerative diseases such as Parkinson's disease and Parkinson's-like syndromes such as progressive supranuclear palsy and multiple system atrophy, senile dementia such as Alzheimer's disease, depression, AIDS encephalopathy, multiple sclerosis, amyotrophie lateral sclerosis, migraine, attention deficit disorder, narcolepsy), sleep apnea or other disorders that cause excessive daytime sleepiness, Huntington's disease, cerebral ischemia, brain trauma, hepatic fibrosis, cirrhosis, and fatty liver.

The scope of the claims is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 1 and 7. The instant compounds are disclosed have adenosine A_{2a} inhibitory or modulatory activity and it is recited that the instant compounds are useful in treating several diseases, for which applicants provide no competent evidence. "Reading specification it appears that instant compound is useful for treating all sorts of diseases including central nervous system diseases such as Alzheimer's disease, Huntington's disease, dementia, amylotrophic

lateral sclerosis etc. for which applicants have not provided any experimental support. Moreover many if not most of central nervous system diseases such as Alzheimer's disease, ALS, multiple sclerosis etc. are very difficult to treat. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition".

To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

That a single class of compounds can be used to prevent any or all diseases in general embraced in the claims is an incredible finding for which applicants have not provided supporting evidence.

Even a recent review of adenosine receptors suggest the use of these antagonists still under experimental stage and speculative in nature. See Baraldi et al., European Journal of Medicinal Chemistry 38: 367-382, 2003.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In

re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The state of the art is indicative of the requirement for undue experimentation.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating various central nervous diseases that require Adenosine A_{2a} inhibitory or modulatory activity.

2) The state of the prior art: A very recent publication expressed that the effects of Adenosine A_{2a} inhibitory activity are still in experimental stage and are unpredictable. See Baraldi et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the treatment or prevention of all or any diseases by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement

obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show all diseases can be treated based on the test results of Adenosine A_{2a} inhibitory activity and the state of the art is that the effects of adenosine receptor antagonists are unpredictable.

6) The breadth of the claims: The instant claims as recited embrace treatment of any or all diseases as well as all central nervous system diseases.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or

use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 25-32, 36 and 40-51 rejected under 35 U.S.C. 102(b) as being anticipated by Caulkett et al., EP 0 515 107.

Caulkett et al., teaches several azolo(1,3,5) triazines as adenosine antagonists useful for treating migraine, which include instant compounds, composition and method of use. See formula I and note the definition of $R^1$and R^2. See pages 2-8 for various embodiments. See pages 9-13 for examples 1-18 for compounds made. Note the compounds taught therein include instant compounds.

Claims 1, 25-32, 36 and 40-51 rejected under 35 U.S.C. 102(b) as being anticipated by Caulkett et al., EP 0 459 702.

Caulkett et al., teaches several azolo(1,3,5) triazines as adenosine antagonists useful for treating migraine, which include instant compounds, composition and method of use. See formula I and note the definition of Q, $R^1$and R^2. See pages 2-11 for

various embodiments. See pages 12-36 for examples 1-175, which include instant compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 25-32, 36 and 40-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caulkett et al., EP 0 515 107.

Teachings of Caulkett et al., as discussed in the above 102 rejection is incorporated herein. As noted above, Caulkett et al., teaches several azolo(1,3,5) triazines as adenosine antagonists useful for treating migraine, which include instant compounds, composition and method of use. See formula I and note the definition of $R^1$and R^2. See pages 2-8 for various embodiments. See pages 9-13 for examples 1-18 for compounds made. Note the compounds taught therein include instant compounds.

Caulkett et al., both generically and more specifically teaches instant compounds. However, Caulkett et al., did not teach all the compounds generically claimed for compound of formula I.

But Caulkett et al., teaches equivalency of the compounds taught in pages 9 through 13 with those generically claimed.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula I using teachings of Caulkett et al., et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1, 25-32, 36 and 40-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caulkett et al., EP 0 459 702.

Teachings of Caulkett et al., as discussed in the above 102 rejection is incorporated herein. As noted above, Caulkett et al., teaches several azolo(1,3,5) triazines as adenosine antagonists useful for treating migraine, which include instant

compounds, composition and method of use. See formula I and note the definition of Q, $R^1$and R^2. See pages 2-11 for various embodiments. See pages 12-36 for examples 1-175, which include instant compounds.

Caulkett et al., both generically and more specifically teaches instant compounds. However, Caulkett et al., did not teach all the compounds generically claimed for compound of formula I.

But Caulkett et al., teaches equivalency of the compounds 1-175 taught in pages 12 through 36 with those generically claimed.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula I using teachings of Caulkett et al., et al and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Allowable Subject Matter

Claims 2-24, 33-35 and 37-39 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims, barring finding of any prior art in a subsequent search, would be allowable as prior art search in the related area and prior art of record did not teach or suggest the compounds and composition embraced in these claims.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

11/27/2006